UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

Friday, February 24, 2017

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 3573-RNR
DP Barcode: D437003
Product Name: Arnie

From: Ian Blackwell, Biologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: Jenny Tao, Senior Toxicologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

To: Eric Miederhoff, PM 31/ *Joseph Daniels*
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: The Procter & Gamble Company

FORMULATION FROM LABEL:

PC Code	Active Ingredient(s):	% by wt.
069149	Didecyl dimethyl ammonium chloride (DDAC)	1.65
	Other Ingredient(s):	98.35
	Total:	100.00

I BACKGROUND: The Procter & Gamble Company (P&G) has submitted three acute toxicity studies and waiver requests in support of the registration of their product, *Arnie*, EPA Reg. No. 3573-RNR. The submitted label describes this product as a soft surface (fabric) sanitizer, deodorizer and fungistat. The submitted documents are provided in the following table:

Study	MRID Number	Document Type
Acute Oral Toxicity	50107407	Study
Acute Dermal Toxicity	50107408	Study
Acute Inhalation Toxicity	50107409	Waiver Request
Primary Eye Irritation	50107406	Waiver Request
Primary Skin Irritation	50107410	Study
Dermal Sensitization	50107406	Waiver Request

The registrants have requested a waiver of the acute inhalation toxicity study (MRID 50107409) based on the following:

1. *Arnie* is to be sold only for use with an automatic closed-loop delivery system. When used as designed, this system is thought to prevent exposure to the concentrated version of this product.
2. The plug in the bottle is a one-way valve and is only available when the dispensing cap is attached to the bottle.
3. The closed-loop system dilutes 3573-RNR five times prior to its delivery of the product.

The registrants have also requested waivers of the primary eye irritation and dermal sensitization studies (MRID 50107406). The registrant requested to assign a toxicity category I for primary eye irritation, and, to classify as a dermal sensitizer, based upon the formulation of the subject product.

The Procter & Gamble Company has also addressed acute toxicity data requirements for the 1:5 use-dilution in MRID 50107411. The registrant stated that the end-use dilution of 3573-RNR is Substantially Similar to their product, *Vesta*, EPA Reg. No. 3573-99.

II RECOMMENDATIONS:

1. The acute oral and dermal toxicity studies are acceptable.

2. The Chemistry and Toxicology Team (CTT) denies the request for a waiver of the acute inhalation toxicity study. We recognize that the product is to be sold for use as part of a closed-loop system; however, the Agency must concern accidental spills and other emergencies. The Agency has no policy wherein we waive acute inhalation toxicity studies because a product is only for use as part of a closed-loop system. The acute inhalation toxicity remains as a data gap.

3. CTT waives the primary eye irritation study and classifies the product toxicity category I due to the percentage of DDAC in this product. In the future, if the registrant develops new data demonstrating that this product should be assigned a toxicity category other than I, CTT will take it into consideration.

4. The primary skin irritation study is acceptable.

5. CTT waives the dermal sensitization study and classifies the product as a dermal sensitizer.

6. CTT finds the 1:5 use-dilution of 3573-RNR to be Substantially Similar to *Vesta*, EPA Reg. No. 3573-99. The acute toxicity profile for *Vesta*, EPA Reg. No. 3573-99 from the previous review on 11/12/13 (D413018) is cited to support precautionary labeling for the 1:5 use-dilution of 3573-RNR.

The acute toxicity profile for File Symbol 3573-RNR (concentrated) is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	50107407	IV	Acceptable
Acute Dermal Toxicity	50107408	III	Acceptable
Acute Inhalation Toxicity	50107409	Undetermined	Waiver Denied
Primary Eye Irritation	50107406	I	Waived
Primary Skin Irritation	50107410	III	Acceptable
Dermal Sensitization	50107406	Sensitizer	Waived

The acute toxicity profile for the 1:5 use-dilution of 3573-RNR[1] is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	49081707	IV	Cited
Acute Dermal Toxicity	49081708	IV	Cited
Acute Inhalation Toxicity	49081709	III	Cited
Primary Eye Irritation	49081710	III	Cited
Primary Skin Irritation	49081711	III	Cited
Dermal Sensitization	49081712	Nonsensitizer	Cited

[1] Cited from *Vesta*, EPA Reg. No. 3573-99

III LABELING:

1. The Signal Word is "DANGER", based upon the classification of the primary eye irritation study of the concentrate of 3573-RNR.

2. CTT cannot further prescribe precautionary labeling (precautionary statements or First Aid statements) for the concentrate of 3573-RNR at present time, due to the data gap for the acute inhalation toxicity requirement.

3. The Precautionary Statements for the 1:5 use-dilution are:

   "Harmful if inhaled. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Avoid breathing spray mist. Remove and wash contaminated clothing before reuse. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco."

4. The First Aid statements for the 1:5 use-dilution are:

   First Aid:

   If in eyes:
   -Hold eye open and rinse slowly and gently with water for 15-20 minutes.

-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Up and Down Procedure

Product Manager: 31 **Reviewer**: I. Blackwell
MRID No.: 50107407 **Study Completion Date**: 10/7/2016
Lab Project No.: 20079832

Testing Laboratory: Charles River
Authors: Jason W. Smedley, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: Arnie, "clear colorless, liquid", EPA File Symbol 3573-RNR

Species: Sprague-Dawley rat
Weight: 166 – 224 g **Age**: 8 weeks
Source: Charles River Laboratories

Conclusion:

1. LD_{50} (mg/kg): **Males=** Not tested
Females= > 5,000 mg/kg
Combined= Not tested

2. The estimated LD_{50} is greater than 5,000 mg/kg of body weight
3. Tox. Category: IV **Classification**: Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
500	---	0/1	---
1750	---	0/1	---
5000	---	0/3	---

Observations: Thinning fur on paws.

Gross Necropsy: The lab reported that there were no test substance-related abnormalities.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 31 **Reviewer**: I. Blackwell
MRID No.: 50107408 **Study Completion Date**: 10/7/2016
Lab Project ID.: 20079833

Testing Laboratory: Charles River Laboratories, Inc.
Author: Jason W. Smedley, BS
Quality Assurance (40 CFR §160.12): Included

Test Material: Arnie, "clear colorless liquid", EPA File Symbol 3573-RNR

Species: New Zealand White rabbit
Weight: Males= 2.5-2.7, females= 2.6-3.0 kg **Age**: 13 weeks
Source: Charles River Laboratories, Inc.

Summary:

1. **LD_{50} (mg/kg)**:

Males	> 2,000 mg/kg
Females	> 2,000 mg/kg
Combined	> 2,000 mg/kg

2. **The estimated LD_{50} is greater than 2,000 mg/kg of body weight.**

3. **Tox. Category**: III **Classification**: Acceptable

Procedure (Deviation From §81-2):

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER DEATHS/NUMBER TESTED)		
	Males	**Females**	**Combined**
2,000	0/5	0/5	0/10

Observations: Erythema, edema, dermal lesions, blanching and/or eschar.

Gross Necropsy Findings: There were no internal findings. Scabs, scales, skin flaking, eschar.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 31 **Reviewer**: I. Blackwell
MRID No.: 50107410 **Study Completion Date**: 10/7/2016
Lab Project ID: 20079834

Testing Laboratory: Charles River
Study Director: Jason W. Smedley, BS

Quality Assurance (40 CFR §160.12): Included

Test Material: Arnie, "clear colorless liquid". EPA File Symbol 3573-RNR
Dosage: 0.5 mL

Species: New Zealand White rabbit
Weight: 2.8 – 3.0 kg **Age**: 16 weeks
Source: Charles River Laboratories, Inc.

Summary:

1. **Toxicity Category**: III

2. **Classification**: Acceptable

Procedure (Deviations from §81-5): None

Results: One-hour after exposure to the test substance the lab observed very slight erythema at 3/3 test sites, which progressed to well-defined erythema at 2/3 test sites by the 24-hour scoring interval. Seventy-two hours after the exposure, 1/3 animals had well-defined erythema and 2/3 had very slight erythema. The dermal irritation resolved completely at 1/3 test sites by the Day 7 scoring interval and in the remaining 2/3 test sites by the Day 14 scoring interval. Additional dermal findings included desquamation (2/3 test sites) on Day 14.

Special Comments: None